



NEWS RELEASE

# Merck Enters into Voluntary Licensing Agreements for Doravirine to Expand Patient Access in Resource-Limited Settings

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Agreements Provide Licenses to Manufacture and Distribute Generic Doravirine for People Living with HIV-1 in More Than 80 Countries

KENILWORTH, N.J., SEPTEMBER 29, 2020 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, has entered into non-exclusive voluntary licensing agreements with two leading generic manufacturers for doravirine (100 mg), the company's oral non-nucleoside reverse transcriptase inhibitor (NNRTI) indicated for the treatment of HIV-1 infection in adults. Under the agreement, Merck will provide licenses for the registration, commercialization, and distribution of generic doravirine (100 mg) for use in a single entity tablet and in a fixed-dose combination tablet with lamivudine (3TC, 300 mg) and tenofovir disoproxil fumarate (TDF, 300 mg) in 86 countries, including all countries of sub-Saharan Africa, other low- and lower middle-income countries outside of sub-Saharan Africa (as classified by the World Bank), and all Least Developed countries (as defined by the United Nations). Merck offers doravirine as the single entity tablet, PIFELTRO™ (doravirine 100 mg), used in combination with other antiretrovirals (ARVs), and in the fixed dose combination tablet, DELSTRIGO™ (doravirine 100 mg/lamivudine 300 mg/tenofovir disoproxil fumarate 300 mg).

“For more than 30 years, Merck has been committed to advancing the treatment and care for people living with HIV, and that commitment includes addressing the health disparities and inequities that challenge underserved populations,” said Dr. Julie L. Gerberding, executive vice president and Chief Patient Officer, Merck. “These voluntary licenses will increase access to additional options in countries hardest hit by the epidemic and reflect Merck’s unwavering commitment to people living with HIV around the world, as well as the continued importance of

collaboration and partnerships.”

Under the terms of the non-exclusive agreements, the licensee companies can manufacture and supply generic doravirine (100 mg) and the fixed-dose combination of doravirine (100 mg)/lamivudine (300 mg)/tenofovir disoproxil fumarate (300 mg) in the 86 countries, including all sub-Saharan African nations. Nearly 80% of people living with HIV globally reside in these 86 countries.

According to UNAIDS, 38 million people were estimated to be living with HIV worldwide at the end of 2018, with a vast majority of those people residing in low- and middle-income countries, but only an estimated 24.5 million people were accessing antiretroviral therapy as of June 2019. There are also 1.7 million additional HIV infections occurring each year.

PIFELTRO is indicated in combination with other antiretroviral (ARV) agents for the treatment of HIV-1 infection in adult patients with no prior ARV treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to doravirine.

DELSTRIGO is indicated as a complete regimen for the treatment of HIV-1 infection in adult patients with no prior ARV treatment history or to replace the current ARV regimen in those who are virologically suppressed (HIV-1 RNA less than 50 copies per mL) on a stable ARV regimen with no history of treatment failure and no known substitutions associated with resistance to the individual components of DELSTRIGO.

#### Selected Safety Information about PIFELTRO and DELSTRIGO

##### Warning: Posttreatment Acute Exacerbation of Hepatitis B (HBV)

All patients with HIV-1 should be tested for the presence of HBV before initiating ARV therapy. Severe acute exacerbations of HBV have been reported in patients who are coinfecting with HIV-1 and HBV and have discontinued products containing lamivudine or tenofovir disoproxil fumarate (TDF), which are components of DELSTRIGO. Patients coinfecting with HIV-1 and HBV who discontinue DELSTRIGO should be monitored with both clinical and laboratory follow-up for at least several months after stopping DELSTRIGO. If appropriate, initiation of anti-HBV therapy may be warranted.

PIFELTRO and DELSTRIGO are contraindicated when co-administered with drugs that are strong cytochrome P450 (CYP)3A enzyme inducers (including the anticonvulsants carbamazepine, oxcarbazepine, phenobarbital, and phenytoin; the androgen receptor inhibitor enzalutamide; the antimycobacterials rifampin and rifapentine; the cytotoxic agent mitotane; and the herbal product St. John's wort (*Hypericum perforatum*)), as significant decreases

in doravirine plasma concentrations may occur, which may decrease the effectiveness of DELSTRIGO and PIFELTRO.

DELSTRIGO is contraindicated in patients with a previous hypersensitivity reaction to lamivudine.

Renal impairment, including cases of acute renal failure and Fanconi syndrome, have been reported with the use of TDF. DELSTRIGO should be avoided with concurrent or recent use of a nephrotoxic agent (e.g., high-dose or multiple NSAIDs). Cases of acute renal failure after initiation of high-dose or multiple NSAIDs have been reported in patients with risk factors for renal dysfunction who appeared stable on TDF.

Prior to or when initiating DELSTRIGO, and during treatment, assess serum creatinine, estimated creatinine clearance, urine glucose, and urine protein in all patients. In patients with chronic kidney disease, also assess serum phosphorus. Discontinue DELSTRIGO in patients who develop clinically significant decreases in renal function or evidence of Fanconi syndrome. Discontinue DELSTRIGO if estimated creatinine clearance declines below 50 mL/min.

In clinical trials in HIV-1 infected adults, TDF was associated with slightly greater decreases in bone mineral density (BMD) and increases in biochemical markers of bone metabolism. Serum parathyroid hormone levels and 1,25 Vitamin D levels were also higher. Cases of osteomalacia associated with proximal renal tubulopathy have been reported with the use of TDF.

Immune reconstitution syndrome can occur, including the occurrence of autoimmune disorders with variable time to onset, which may necessitate further evaluation and treatment.

Because DELSTRIGO is a complete regimen, co-administration with other antiretroviral medications for the treatment of HIV-1 infection is not recommended.

Co-administration of PIFELTRO with efavirenz, etravirine, or nevirapine is not recommended.

If DELSTRIGO is co-administered with rifabutin, take one tablet of DELSTRIGO once daily, followed by one tablet of doravirine (PIFELTRO) approximately 12 hours after the dose of DELSTRIGO.

If PIFELTRO is co-administered with rifabutin, increase PIFELTRO dosage to one tablet twice daily (approximately 12 hours apart).

Consult the full Prescribing Information prior to and during treatment for more information on potential drug-drug interactions.

Because DELSTRIGO is a fixed-dose combination tablet and the dosage of lamivudine and TDF cannot be adjusted,

DELSTRIGO is not recommended in patients with estimated creatinine clearance less than 50 mL/min.

The most common adverse reactions with DELSTRIGO (incidence  $\geq 5\%$ , all intensities) were dizziness (7%), nausea (5%), and abnormal dreams (5%). The most common adverse reactions with PIFELTRO (incidence  $\geq 5\%$ , all intensities) were nausea (7%), dizziness (7%), headache (6%), fatigue (6%), diarrhea (6%), abdominal pain (5%), and abnormal dreams (5%).

By Week 96 in DRIVE-FORWARD, 2% of adult subjects in the PIFELTRO group and 3% in the DRV+r group had adverse events leading to discontinuation of study medication.

By Week 96 in DRIVE-AHEAD, 3% of adult subjects in the DELSTRIGO group and 7% in the EFV/FTC/TDF group had adverse events leading to discontinuation of study medication.

In DRIVE-FORWARD, mean changes from baseline at Week 48 in LDL-cholesterol (LDL-C) and non-HDL-cholesterol (non-HDL-C) were pre-specified. LDL-C: -4.6 mg/dL in the PIFELTRO group vs 9.5 mg/dL in the DRV+r group. Non-HDL-C: -5.4 mg/dL in the PIFELTRO group vs 13.7 mg/dL in the DRV+r group. The clinical benefits of these findings have not been demonstrated.

In DRIVE-AHEAD, mean changes from baseline at Week 48 in LDL-C and non-HDL-C were pre-specified. LDL-C: -2.1 mg/dL in the DELSTRIGO group vs 8.3 mg/dL in the EFV/FTC/TDF group. Non-HDL-C: -4.1 mg/dL in the DELSTRIGO group vs 12.7 mg/dL in the EFV/FTC/TDF group. The clinical benefits of these findings have not been demonstrated.

In DRIVE-SHIFT, mean changes from baseline at Week 48 in LDL-C and non-HDL-C were pre-specified. LDL-C: -16.3 mg/dL in the DELSTRIGO group vs -2.6 mg/dL in the PI + ritonavir group. Non-HDL-C: -24.8 mg/dL in the DELSTRIGO group vs -2.1 mg/dL in the PI + ritonavir group. The clinical benefits of these findings have not been demonstrated.

In DRIVE-AHEAD, neuropsychiatric adverse events were reported in the three pre-specified categories of sleep disorders and disturbances, dizziness, and altered sensorium. Twelve percent of adult subjects in the DELSTRIGO group and 26% in the EFV/FTC/TDF group reported neuropsychiatric adverse events of sleep disorders and disturbances; 9% in the DELSTRIGO group and 37% in the EFV/FTC/TDF group reported dizziness; and 4% in the DELSTRIGO group and 8% in the EFV/FTC/TDF group reported altered sensorium.

The safety of DELSTRIGO in virologically-suppressed adults was based on Week 48 data from subjects in the DRIVE-SHIFT trial. Overall, the safety profile in virologically-suppressed adult subjects was similar to that in subjects with no ARV treatment history.

There is a pregnancy exposure registry that monitors pregnancy outcomes in individuals exposed to PIFELTRO or

DELSTRIGO during pregnancy. Healthcare providers are encouraged to register patients by calling the Antiretroviral Pregnancy Registry (APR) at 1-800-258-4263.

Mothers infected with HIV-1 should be instructed not to breastfeed if they are receiving PIFELTRO or DELSTRIGO due to the potential for HIV-1 transmission.

#### Our Commitment to HIV

For more than 30 years, Merck has been committed to scientific research and discovery in HIV, and we continue to be driven by the conviction that more medical advances are still to come. Our focus is on pursuing research that addresses unmet medical needs and helps people living with HIV and their communities. We remain committed to working hand-in-hand with our partners in the global HIV community to address the complex challenges that hinder continued progress.

#### About Merck

For more than 125 years, Merck, known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases in pursuit of our mission to save and improve lives. We demonstrate our commitment to patients and population health by increasing access to health care through far-reaching policies, programs and partnerships. Today, Merck continues to be at the forefront of research to prevent and treat diseases that threaten people and animals – including cancer, infectious diseases such as HIV and Ebola, and emerging animal diseases – as we aspire to be the premier research-intensive biopharmaceutical company in the world. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on **Twitter**, **Facebook**, **Instagram**, **YouTube** and **LinkedIn**.

#### Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company's management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of the global outbreak



of novel coronavirus disease (COVID-19); the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company's ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company's patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in the company's 2019 Annual Report on Form 10-K and the company's other filings with the Securities and Exchange Commission (SEC) available at the SEC's Internet site ([www.sec.gov](http://www.sec.gov)).

Please see Prescribing Information for PIFELTRO (doravirine) at:

[https://www.merck.com/product/usa/pi\\_circulars/p/pifeltro/pifeltro\\_pi.pdf](https://www.merck.com/product/usa/pi_circulars/p/pifeltro/pifeltro_pi.pdf); and Patient Information for PIFELTRO (doravirine) at: [https://www.merck.com/product/usa/pi\\_circulars/p/pifeltro/pifeltro\\_ppi.pdf](https://www.merck.com/product/usa/pi_circulars/p/pifeltro/pifeltro_ppi.pdf)

Please see Prescribing Information for DELSTRIGO (doravirine/3TC/TDF)

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